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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/920,068	08/01/2001	Eckhard Wolf	50125/015002	4409

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EXAMINER	
GOLDBERG, JEANINE ANNE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 02/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/920,068	WOLF ET AL.	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-79* is/are pending in the application.

4a) Of the above claim(s) *1-23,25-27,31 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,24,28-30 and 33-79* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed December 8, 2003. Currently, claims 1-79 are pending. Claims 1-23, 25-27, 31-32 have been withdrawn as drawn to non-elected subject matter.

Election/Restrictions

2. Applicant's election without traverse of Group XI in the paper filed December 8, 2003 is acknowledged. The response selects XW1695, SEQ ID NO: 4 for examination. The applicants indicate that this is a species election, however it is noted that the examiner set forth a restriction between the sequences. Thus, upon examination of SEQ ID NO: 4, no additional sequences will be examined.

The requirement is still deemed proper and is therefore made FINAL.

Priority

3. This application claims priority to provisional application 60/229,501, filed August 31, 2000 and foreign priority to Germany 10038111.1, filed August 4, 2000.

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of an interference, a translation of the foreign application should be submitted under 37 CFR 1.55 in reply to this action.

Drawings

4. The drawings are acceptable.

Claim Rejections - 35 USC § 112- Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 23-24, 28-30, 33-79 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

<u>The nature of the invention and breadth of claims</u>

The claims are broadly drawn to a method of diagnosing, predisposing and/or treating a skin disease, any skin disease, by measuring the amount of the G-protein coupled receptor-polypeptide of SEQ ID NO: 4. The invention is an class of invention

which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The unpredictability of the art and the state of the prior art

The art teaches human SW1695 as IGS3 GPCR and Ant GPCR, for example. The prior art teaches a nucleic acid sequence of IGS3 which is identical to SEQ ID NO: 4. Deleersnijder et al.(WO01/19983, March 2001) teaches IGS3 may be used in array technology methods to address a variety of questions in molecular genetics (page 18-19). Moreover, Lind et al. (US 2002/0062013, May 23, 2002) teaches nGPCR-x and methods of using the receptors. SEQ ID NO: 11 of Lind is 100% identical to the instant sequence.

The art teaches a very broad class of diseases which are considered skin diseases or dermatology diseases. For example, The Skin Site teaches that acne, boils, Candida, cysts, Grover's disease, hair loss, heat rash, Lyme disease, psoriasis, ring worm, skin tags, shingles, dandruff, eczema, moles, cancer are all forms of skin diseases. Upon reviewing each of these diseases, it is clear that each of these diseases has a different mode of invasion, and mechanisms which control the disease. For example Candida is a microorganism, Grover's disease's cause is unknown, moles tend to be inherited, Schamberg's disease is caused by people with leaky blood vessel walls, and acne is caused by oil glands.

Working Examples

The specification has no working examples of diagnosing, predisposing or treating any particular patient by quantifying the amount of SEQ ID NO: 4 in a sample.

Guidance in the Specification.

The specification teaches the level of expression of SW1695 in badly healing wounds of dexamethasone treated mice was three times the level of expression in the wounds of control mice. The specification also states that human SW1695 was found to be dysregulated in psoriatic skin: a significantly higher expression of the gene was found in non-affected skin biopsies of psoriasis patients compared to lesional, affected skin of the same patient, which evidences that dysregulation of gene expression of these genes can be a diagnostic of and can also cause skin disorders, especially psoriasis (page 9).

SW1695 was asserted to be regulated in wounds. A three fold higher amount of SW1695 was measured in poorly healing wounds of animals treated with dexamethasone than in wounds of control animals (page 45).

The specification states that SW1695 is relatively reduced in level of expression by 60-70% in day 1 and day 5 normal healing wound relative to whereas SW1695 mRNA could not be detect in the wound ground or in the wound edge. The specification asserts that this dysregulation of SW1695 expression, especially the lack of mRNA can lead to severe wound healing disorders (page 49).

The specification describes the expression of SW1695 in psoriasis patients. As seen in Figure 2 and 3, SW1695 mRNA was set to 1.00 in intact skin of healthy persons. The relative amount of SW1695 in unaffected, non-lesional skin of psoriasis is 3.8 whereas the amount in affected, lesional psoriatic skin is 1.1. The specification asserts that this can be sued as a marker for psoriasis predisposition in unlesional skin displays, as SW1695 displays an increased amount of SW1695 mRNA expression compared to skin of healthy persons (page 51).

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant number of parameters which would have to be studied to apply this technology for diagnosis, prevention and/or treatment of the full scope of the claims.

Given the teachings in the specification, it is unpredictable that SW1695, a nucleic acid encoding SEQ ID NO: 4, would be able to diagnose and/or treat psoriasis. The specification describes an example of determining the abundance of SW1695 mRNA in individual biopsies. The specification describes a total of 2 biopsies of intact skin of healthy subjects and 4 biopsies in each case of lesional and non-lesional skin from psoriasis patients (page 51). It is noted that a sample size of 2 control subjects is a very small sample size. The specification fails to provide any teachings as to how many biopsies from psoriasis patients were used. Thus, it is unclear whether the sample size used would yield any particularly significant results. Assuming that the sample size was large enough to provide meaningful results, the specification teaches that the mRNA was normalized for control individuals to 1.0. The relative amount in unaffected, non-lesional skin of psoriasis is 3.8 whereas the amount in affected, lesional psoriatic skin is 1.11 (page 51). Given this information, taking a sample from a normal individual and a sample from a lesional psoriatic skin, there is no difference in expression levels between the two samples. The specification fails to assert any particular significant association. Further the claims are not limited to sampling of non-lesional skin of psoriasis individuals. Additionally, it is unclear whether the overexpression in non-lesional psoriasis patients is due to psoriasis or whether the overexpression is general to all types of skin lesions. There is no guidance in the specification whether the overexpression also affects individuals with acne, shingles or

dermatis. Given the teachings in the specification, the skilled artisan would be required to perform additional experimentation to ascertain how to use the claims as broadly as written.

With respect to wound healing, the specification appears to be directed to analysis in murine individuals. There is no particular examples of wound healing using a nucleic acid of SEQ ID NO: 4. The specification teaches that "a three fold higher amount of SW1695 was measure in poorly healing wounds of animals treated with dexamethasone than in wounds of control animals." Examples of skin biopsies of untreated intact skin and untreated one and five day wounds of healthy trial participants were used (page 45). The specification continues to teach a 60% decrease in SW1695 in one day wounds as opposed to intact skin. This suggest that the expression of SW1695 is lower in wounds than in intact skin.

Taking the specification as a whole, it is unpredictable whether skin lesions will have increased or decreased expression as compared to normal skin. For example, in psoriasis, the specification asserts that the expression is increased, however in wounds the expression is decreased. There is no predictable association between the expression levels of nucleic acid encoding SEQ ID NO: 4 and skin lesions or skin diseases.

As discussed above, the genus of skin diseases is sufficiently large such that prior to making any particular extrapolation for information provided in the instant specification, significant further undue and unpredictable experimentation would be required. It is unpredictable as to whether one could successfully use the claimed invention, and given the fact that neither the specification nor the prior art provide evidence of a correlation or association between a nucleic acid encoding SEQ ID NO: 4 expression and the large genus of skin diseases, it is further unpredictable as to

whether any quantity of experimentation would allow one to practice the claimed invention as broadly as claimed. While one could conduct additional experimentation to determine whether, e.g., expression of nucleic acid encoding SEQ ID NO: 4 at certain levels might be associated with, e.g. certain types of skin diseases, the outcome of such research cannot be predicted and such further research and experimentation are both unpredictable and undue. Accordingly, it would require undue experimentation for a skilled artisan to use the claimed invention.

This would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, in a highly unpredictable art to determine whether expression of a nucleic acid of SEQ ID NO: 4 within skin lesions is overexpressed or underexpressed as compared with normal tissues. Further, the prior art and the specification provides insufficient guidance to overcome problems of determine whether expression is associated with diseases. As explained above, the broad class of skin diseases encompassed by the instant claims all have a different mechanism and mode of infection. The identification of a single mode or mechanism which may be applicable to a single disease would not be expected to be the same mechanism for all possible skin diseases. As discussed above, the genus of skin diseases is caused by a variety of different means which do not appear to be genetic in

nature. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 24, 28-30, 33-79 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 24, 29, 30, 33, 34 provide for the use of a G-protein coupled receptor-polypeptide according to the sequence of SEQ ID NO: 4 for diagnosis, prevention and/or treatment of skin disease, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

B) Claim 28, 29, 30, 33-34 provide for the use of a G-protein coupled receptor-polypeptide according to the sequence of SEQ ID NO: 4 for the production of an array fixated to a carrier material for the analysis of skin disease, but, since the claim does not

set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

C) Claims 35-79 are indefinite because it is unclear as to whether the claims are intended to be limited to methods of diagnosing a skin disease in a patient or a method of identifying a nucleic acid encoding SEQ ID NO: 4. The claims are drawn to a method of diagnosing a skin disease in a patient, however the final step is one of identifying a nucleic acid. Accordingly, it is unclear whether the claimed method is one for diagnosing skin disease or a method of identifying a nucleic acid encoding SEQ ID NO: 4. In claims 36 and 37 the claims are drawn to determining the amount of SEQ ID NO: 4, however it is unclear how the amount of the nucleic acid aids in the diagnosis of skin disease. Further Claim 37 is directed to comparing the amount of nucleic acids, however, it is unclear how the skilled artisan would diagnosis disease based upon the results of the analysis. The claims could be more clear and definite if the final step indicated "wherein the over expression of SEQ ID NO: 4 as compared to .... Is indicative of skin disease," for example. Moreover, the Claims 50 and 64 are similarly unclear as to the method steps and how they achieve the intended use of the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 24, 28 are rejected under 35 U.S.C. 102(a) as being anticipated by Deleersnijder et al.(WO01/19983, March 2001).

It is noted that the priority claims to the provisional application and the foreign document are not award for the reasons set forth above.

Further, this claim has been treated as a method for using a G-protein coupled receptor-polypeptide of SEQ ID NO: 4. The clause directed to "for diagnosis, prevention and/or treatment" has been deemed an intended use clause and has not been afforded any particular weight.

Deleersnijder teaches IGS3 may be used in array technology methods to address a variety of questions in molecular genetics (page 18-19). IGS3 is 100% identical to a nucleic acid encoding SEQ ID NO: 4. Since Deleersnijder teaches a method of using SEQ ID NO: 4, Deleersnijder anticipates the claimed invention.

8. Claims 24, 28 are rejected under 35 U.S.C. 102(a) as being anticipated by

It is noted that the priority claims to the provisional application and the foreign document are not award for the reasons set forth above.

Further, this claim has been treated as a method for using a G-protein coupled receptor-polypeptide of SEQ ID NO: 4. The clause directed to "for diagnosis, prevention

and/or treatment" has been deemed an intended use clause and has not been afforded any particular weight.

Lind et al. (herein referred to as Lind) teaches a nucleic acid, namely SEQ ID NO: 11 which is 100% identical to the instant sequence. Lind teaches placing the nucleic acids on an array for expression analysis (for example para 332).

Conclusion

9. No claims allowable.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 6:00 a.m. to 3:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (571)272-0507

J. Goldberg

Jeanine Goldberg
Patent Examiner
February 4, 2004